

OBESITY, WEIGHT DISTRIBUTION AND RISK OF ACUTE KIDNEY INJURY IN  
THE ATHEROSCLEROSIS RISK IN COMMUNITIES (ARIC) STUDY

by

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## ABSTRACT

Background: Elevated body mass index (BMI) has been associated with acute kidney injury (AKI) in surgical and critically ill patients. Less is known about the relationship between obesity and AKI in the population-based setting.

Study Design: Prospective cohort study.

Setting & Participants: Participants of the Atherosclerosis Risk in Communities (ARIC) study who attended a study visit between 1996 and 1998.

Predictors: BMI and waist-to-hip ratio (WHR) at baseline.

Outcome: AKI occurring during subsequent hospitalizations.

Measurements: Cox proportional hazards models included the following variables: BMI (modeled as a linear spline, with knot at 30 kg/m<sup>2</sup>), WHR, age, sex, race, hypertension, diabetes, coronary artery disease, estimated glomerular filtration rate, and albuminuria. Participants were censored at 12/31/2010, death, or end-stage renal disease.

Results: At baseline, participants' mean age was 63.3 years, mean BMI was 28.8 kg/m<sup>2</sup>, and mean WHR was 0.92 for women and 0.98 for men. Over 12 years of follow-up, 824 participants developed AKI. There was a U-shaped relationship between BMI and AKI.

For BMI > 30 kg/m<sup>2</sup>, a 1 kg/m<sup>2</sup> increase was associated with a 7% increase in risk of AKI (adjusted hazard ratio (aHR) 1.07, 95% CI: 1.06, 1.09, p < 0.001); for BMI < 30 kg/m<sup>2</sup>, a 1 kg/m<sup>2</sup> increase was associated with a 3% decrease in AKI risk (aHR 0.97, 95% CI: 0.94, 0.99, p = 0.04). Elevated WHR was linearly associated with AKI. A 0.01 increase in WHR was associated with a 3% increase in risk of AKI (aHR 1.03, 95% CI: 1.01, 1.04; p < 0.001). There was no statistically significant interaction between WHR and BMI.

Limitations: BMI and WHR were measured only at baseline.

Conclusions: In a population-based cohort, higher BMI over 30 kg/m<sup>2</sup> and higher WHR were independently associated with increased risk of hospitalized AKI. Obese individuals may benefit from strategies to prevent AKI.

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## INTRODUCTION

Obesity has reached epidemic proportions worldwide. In the United States, nearly 35% of adults were obese ( $\text{BMI} \geq 30 \text{ kg/m}^2$ ) and another 33% were overweight ( $\text{BMI} 25\text{-}29.9 \text{ kg/m}^2$ ) in 2012 (1). Accompanying the rise in obesity is a rise in prevalence of many obesity-related complications, including chronic kidney disease (2-4). There is some evidence to suggest that obese surgical and critically ill patients face higher risk of acute kidney injury (AKI) (5-11). This relationship has not been studied in broader populations. As no specific therapies for AKI are available, prevention of avoidable cases is key. Discovery of new risk factors for AKI may help to identify individuals who might benefit from preventive strategies.

Body mass index (BMI) is the most widely utilized measure of obesity, but it may not be the best measure of adiposity (12). Central measures of adiposity, such as waist to hip ratio, waist circumference, and waist to height ratio, are thought to be better indicators of visceral adiposity (13, 14). In several studies, one or more central measures of adiposity have been shown, independent of BMI, to be associated with outcomes such as all-cause mortality (15, 16), cardiovascular disease (17, 18), hypertension (19), and diabetes (20, 21). Other studies have shown that central adiposity measures may be better predictors of outcomes compared to BMI (22-25). Whether a measure of abdominal adiposity may provide additional information regarding risk of AKI compared to BMI alone is unknown.



The Atherosclerosis Risk in Communities (ARIC) study is a prospective, community-based cohort of 15,792 participants enrolled between 1987 and 1989. Using participants who presented for visit 4 (1996 to 1998), we examined whether BMI and waist-to-hip ratio were risk factors for subsequent hospitalized AKI, independent of established risk factors for AKI. We also evaluated whether the relationship of obesity with AKI identified by diagnostic codes (which are known to have low sensitivity) was similar to that defined by change in creatinine according to Kidney Disease: Improving Global Outcomes (KDIGO) in a subset of the ARIC population.

## METHODS

### *Study Population*

The ARIC study is a prospective, community-based cohort of individuals aged 45 to 64 at enrollment from four communities (Washington County, MD; Forsyth County, NC; Jackson, MS; and Minneapolis, MN) (26). A total of 15,792 individuals were initially enrolled between 1987 and 1989, and then re-examined at the second (1990-1992), third (1993-1995), fourth (1996-1998) and fifth (2011-2013) visits. Although BMI and WHR were measured at each exam, albuminuria (a significant risk factor for AKI) was first measured at the fourth exam; thus, the fourth study visit (visit 4) was treated as the baseline for the present study. Of the 11,656 participants attending visit 4, 11,063 were included in our analysis. Participants were excluded for the following reasons: previous episode of AKI or estimated glomerular filtration rate (eGFR)  $< 15$  ml/min/1.73 m<sup>2</sup> (N = 52), missing BMI (N = 38), missing WHR (N = 1), WHR  $> 1.5$  (N = 4), or missing data on one or more other covariates (N = 498).

### *Measurements and Definitions*

Weight and height assessed at the baseline visit (visit 4) were used to calculate BMI. Obesity was defined as BMI  $\geq 30$  kg/m<sup>2</sup>. Waist and hip circumference were also measured at the baseline visit, and WHR was defined as their ratio. There are no universally accepted cut-offs for WHR. The World Health Organization has reported

substantially increased risk of metabolic complications for women with WHR  $\geq 0.85$  and  $\geq 0.90$  for men (27); however, in the ARIC study, > 90% of male participants had a WHR  $\geq 0.90$ . Thus, for our analysis, a WHR  $\geq 0.85$  in women and WHR  $\geq 0.95$  in men was considered elevated. Diabetes was defined as a single fasting serum glucose  $\geq 126$ mg/dL, non-fasting glucose  $\geq 200$  mg/dL, use of antidiabetic medications, or patient-reported diagnosis of diabetes. Hypertension was defined as systolic blood pressure  $\geq 140$  mmHg, diastolic blood pressure  $\geq 90$  mmHg (from a mean of two blood pressure measurements), or use of antihypertensive agents. Creatinine was measured by the modified kinetic Jaffe method in plasma samples. Creatinine values were then calibrated to the National Institute of Standards and Technology standard, and eGFR was calculated using the CKD Epidemiology Collaboration (CKD-EPI) 2009 creatinine equation (28). Urine albumin to creatinine ratio (ACR) was measured from a spot urine sample by a nephelometric method. Albuminuria was defined as  $\geq 30$  mg of albumin per gram of creatinine; moderately increased albuminuria was defined as 30-300 mg of albumin per gram of creatinine and severely increased albuminuria was defined as  $> 300$  mg of albumin per gram of creatinine.

#### *AKI Ascertainment*

After enrollment, ARIC participants were followed prospectively for hospitalizations via annual phone interviews (> 90% contact rate at 20 years) and active surveillance of discharge lists from community hospitals. At least 26 distinct diagnostic codes were abstracted from discharge documentation. Deaths were identified through active

surveillance of local newspaper obituaries, state death lists and death certificates from the Department of Vital Statistics. *International Classification of Diseases, 10<sup>th</sup> Revision, Clinical Modification (ICD-10-CM)* codes were abstracted from death certificates. Hospitalization with AKI was defined as the presence of one of the following codes among the discharge diagnoses or causes of death: *International Classification of Diseases, 9<sup>th</sup> Revision, Clinical Modification (ICD-9-CM)* codes 584.x and *ICD-10-CM* codes N17.x. This approach has been previously shown to have high specificity (99.6%) but low to moderate sensitivity (17.4% for any AKI, 40.3% for stage 2-3 AKI) compared to creatinine-based methods using KDIGO criteria (29). AKI hospitalizations that occurred between visit 4 and December 31, 2010 were included in this analysis.

### *Statistical Analysis*

Baseline characteristics of participants were compared by obesity status (BMI < 30 kg/m<sup>2</sup> and ≥ 30 kg/m<sup>2</sup>), and normal and elevated WHR (elevated WHR defined as ≥ 0.85 for women and ≥ 0.95 for men) using  $\chi^2$  and t tests. The association of BMI, WHR and hospitalized AKI, was modeled using Cox proportional hazards regression. Hazard ratios were determined for each 1 kg/m<sup>2</sup> change in BMI and each 0.01 increase in WHR as each represented approximately 15% of their respective standard deviations. Because a non-linear relationship between BMI and hospitalized AKI was observed, BMI was modeled as a linear spline with knot at 30 kg/m<sup>2</sup>. In locally-weighted smoothing plots, WHR demonstrated a fairly linear relationship with hospitalized AKI and thus was modeled as a continuous linear variable. Participants were censored at December 31, 2010, or at the

time of incident end-stage renal disease or death. Analyses were adjusted for age, sex, race, eGFR (modeled as a linear spline with knot at 60 ml/min/1.73 m<sup>2</sup>), log ACR, hypertension, diabetes, and coronary heart disease. To determine whether the relationship between WHR and AKI varied by obesity status, an interaction between obesity and WHR was tested. To evaluate the robustness of the associations by CKD status, analyses were repeated in participants with and without CKD (defined as eGFR < 60 ml/min/1.73 m<sup>2</sup> or eGFR > 60 ml/min/1.73 m<sup>2</sup> with albuminuria).

Several sensitivity analyses were also conducted. First, to assess whether an obesity-AKI association might be driven by the higher frequency of hospitalizations in obese compared to non-obese participants, we included the number of hospitalizations as a time-varying covariate in our model. Second, to assess whether the relationship was simply driven by a higher rate of cardiac interventions in obese participants, we repeated analyses excluding AKI events occurring during cardiac procedures (*ICD-9-CM* codes 00.66, 35.x through 39.x). Third, because diagnostic codes tend to have low sensitivity in the identification of AKI, we repeated analyses in a subset of ARIC participants from Washington County, MD, for whom we had access to system-wide data from the Meritus Health System, identifying AKI cases based on the KDIGO creatinine-based criteria. Finally, to evaluate whether the obesity-AKI relationship was simply driven by more rapid CKD progression among obese compared to non-obese participants, we modeled the association between BMI, WHR and hospitalized AKI in the subset of Washington County participants using time-varying eGFR as a covariate. All statistical analyses were performed using Stata 13.1 (StataCorp, College Station, TX).

### *Additional Analyses*

To evaluate the association of waist circumference (WC) and hospitalized AKI, Cox proportional hazards regression was also used to model the association between BMI, WC and hospitalized AKI. Models were adjusted for the same covariates mentioned above. An interaction between BMI and WC was also tested. Subgroup analysis and sensitivity analyses were also carried out for WC.

## RESULTS

### *Baseline Characteristics of Participants*

Among the 11,063 participants in the study population, 824 (7.5%) developed hospitalized AKI over a mean follow up of 12.0 years (standard deviation (SD) 3.1 years). Over a third (35%) of participants were obese ( $\text{BMI} \geq 30 \text{ kg/m}^2$ ) at baseline, and 78% of participants had an elevated WHR. Compared to non-obese participants, participants with a  $\text{BMI} \geq 30 \text{ kg/m}^2$  were slightly younger, more often female, and more often black; they were also more likely to have diabetes, hypertension,  $\text{eGFR} < 60 \text{ ml/min/1.73 m}^2$ , and albuminuria (**Table 1**). Despite a higher proportion of participants with  $\text{eGFR} < 60 \text{ ml/min/1.73 m}^2$ , mean eGFR was slightly higher in the obese group. Compared to participants with normal WHR, participants with elevated WHR were slightly older, and more often white; they were also more likely to have diabetes, hypertension,  $\text{eGFR} < 60 \text{ ml/min/1.73 m}^2$ , and albuminuria. Interestingly, there was no difference in prevalent coronary heart disease by BMI or WHR. There was also a substantial number of participants with abnormal BMI and normal WHR, and vice versa: the proportion of participants with elevated BMI was 11.0% among those with normal WHR, and 58.4% of those with elevated WHR had  $\text{BMI} < 30 \text{ kg/m}^2$ .

### *Association between BMI, WHR and hospitalized AKI*

In unadjusted analysis, higher baseline BMI was significantly associated with hospitalized AKI. Below 30 kg/m<sup>2</sup>, each 1 kg/m<sup>2</sup> increase in BMI was associated with a 3% increase in risk of hospitalized AKI (hazard ratio (HR) 1.03, 95% CI: 1.01, 1.06, p = 0.02). Above 30 kg/m<sup>2</sup>, each 1 kg/m<sup>2</sup> increase in BMI was associated with a 7% increase in risk of hospitalized AKI (HR 1.07, 95% CI: 1.06, 1.09, p <0.001). In adjusted analysis (including adjustment for WHR), there was a U-shaped relationship between BMI and hospitalized AKI, with the risk of hospitalized AKI decreasing for each 1 kg/m<sup>2</sup> increase in BMI below 30 kg/m<sup>2</sup> (adjusted HR (aHR) 0.97, 95% CI: 0.94, 1.00, p = 0.04) but increasing for each 1 kg/m<sup>2</sup> increase in BMI above 30 kg/m<sup>2</sup> (aHR 1.07, 95% CI: 1.06, 1.09, p <0.001) (**Figure 1**). All covariates included in the full model were also significantly associated with hospitalized AKI.

In unadjusted analysis, higher WHR was also associated with hospitalized AKI (per 0.01 increase, HR 1.06, 95% CI: 1.05, 1.07, p <0.001). In adjusted analysis, each 0.01 increase in WHR was associated with a 3% increase in risk of hospitalized AKI (aHR 1.03, 95% CI: 1.01, 1.04, p <0.001). This association was seen in both men and women (**Figure 2**). The relationship between WHR and AKI was significant in obese populations and marginally significant in non-obese populations (for obese participants, aHR 1.03, 95% CI 1.01, 1.06, p = 0.002; for non-obese participants, aHR 1.02, 95% CI 1.00, 1.03, p = 0.05; p for interaction = 0.4). Demographic adjusted AKI incidence was lowest among participants with BMI < 25 kg/m<sup>2</sup> and WHR below the cutoff and highest among participants with BMI ≥ 30 kg/m<sup>2</sup> and elevated WHR (**Table 3**).



### *Subgroup Analysis*

When stratified by CKD (defined as  $\text{eGFR} < 60 \text{ ml/min/1.73 m}^2$  or  $\text{eGFR} \geq 60 \text{ ml/min/1.73 m}^2$  with albuminuria), hazard ratios for BMI  $> 30 \text{ kg/m}^2$  and hospitalized AKI were similar to those for the entire cohort (**Table 2**). Increasing BMI below  $30 \text{ kg/m}^2$  was protective only among participants with CKD; there was no association between BMI and hospitalized AKI among non-obese participants without CKD. However, a formal test for interaction between BMI and CKD was not statistically significant ( $p = 0.4$ ). The association of WHR and hospitalized AKI was similar in the subgroups, although not significant among those with CKD, likely due to small sample size. There was no interaction between WHR and CKD ( $p = 0.2$ ).

### *Sensitivity Analysis*

When number of hospitalizations was included as a time-varying covariate, the association between BMI and WHR with hospitalized AKI were similar to the original model (**Table 4**). Associations were also similar when excluding the 85 participants with AKI occurring concomitant with a cardiac procedure. In the subset of 2,486 participants who had at least one encounter in the Washington County Meritus Health System, 290 cases of AKI were identified using KDIGO creatinine-based criteria. The association between BMI  $\geq 30 \text{ kg/m}^2$ , WHR, and AKI were similar, although an association of BMI  $< 30 \text{ kg/m}^2$  and hospitalized AKI was no longer observed. Using the same Washington County subset and adjusting for eGFR as a time-varying covariate produced similar

results, although the association of WHR with hospitalized AKI did not reach statistical significance. There was little difference in the associations between baseline eGFR and hospitalized AKI and time-varying eGFR and AKI (aHR for each 1 ml/min/1.73 m<sup>2</sup> increase in baseline eGFR < 60 ml/min/1.73 m<sup>2</sup> 0.95, 95% CI: 0.93, 0.97, p < 0.001; aHR for each 1 ml/min/1.73 m<sup>2</sup> increase in time-varying eGFR < 60 ml/min/1.73 m<sup>2</sup> 0.96, 95% CI: 0.95, 0.97, p < 0.001).

#### *Analyses Involving Waist Circumference*

In unadjusted analysis, WC was associated with hospitalized AKI. Each 2.5 cm increase in WC was associated with a 7% increase in risk of AKI (HR 1.07, 95% CI: 1.06, 1.08, p < 0.001). In adjusted analysis, each 2.5 cm increase in WC was associated with a 5% increase in risk of hospitalized AKI (aHR 1.05, 95% CI: 1.05, 1.10, p < 0.001). In subgroup and sensitivity analyses, WC was not as consistently associated with AKI in comparison to WHR.

## DISCUSSION

In this community-based study of 11,063 participants followed for an average of 12 years, both BMI and WHR were independently associated with hospitalized AKI. While the relationship between WHR was linear, in adjusted analyses, there was a U-shaped relationship between BMI and hospitalized AKI. At  $\text{BMI} \geq 30 \text{ kg/m}^2$ , higher BMI was associated with higher AKI risk. Paradoxically, at  $\text{BMI} < 30 \text{ kg/m}^2$ , higher BMI was associated with lower AKI risk, although this relationship was significant only among persons with baseline CKD. These results suggest that obese individuals and individuals with high WHR should be considered to have increased risk of developing AKI.

This study extends on prior studies that demonstrated a significant relationship between obesity and AKI in various clinical populations. Druml et al studied 5,232 patients in intensive care units and found the odds of AKI requiring renal replacement therapy were increased 1.35 times higher in patients who were overweight, and 2.54 times higher in patients who were obese, compared to normal weight patients (6). Billings et al studied 445 patients undergoing cardiac surgery and found that the odds of AKI (stage I or worse by Acute Kidney Injury Network (AKIN) criteria) increased 26.5% for each  $5 \text{ kg/m}^2$  increase in BMI (5). Shashaty et al studied 400 critically ill trauma patients and found that a  $\text{BMI} > 30 \text{ kg/m}^2$  was associated with an odds ratio of 4.72 for developing AKI (by AKIN criteria) (7). Our study adds to this body of literature by demonstrating a significant relationship between BMI and AKI in a large, population-based cohort. In addition, we report an interesting nuance: a slightly protective effect of higher BMI up to

30 kg/m<sup>2</sup>, particularly in participants with preexisting CKD. This observation may be analogous to decreased mortality rates seen among overweight and mildly obese individuals in the general population (15) and in those with coronary artery disease (30).

Several potential mechanisms might link obesity to kidney injury. Obesity is associated with increased production of adipokines, proinflammatory cytokines, and markers of oxidative stress (5, 31, 32). These have been linked to acute kidney injury, although the mechanisms of injury have yet to be elucidated. Obese individuals may be more susceptible to volume depletion due to difficulty with assessment of volume status, or they may be more likely to receive supratherapeutic doses of nephrotoxic medications such as antibiotics given uncertainty regarding appropriate dosing (31). A possible explanation for the independent association of WHR even after adjustment of BMI, is that both conditions may lead to increased sagittal abdominal diameter and intra-abdominal pressure (33, 34), which has been shown to be associated with AKI (35).

There are several strengths and limitations of this study. This is the first large, population based study of AKI with baseline BMI and WHR measured prior to hospitalization for AKI. Few, if any, studies have assessed WHR or WC as a risk factor for AKI. All data were collected prospectively, and hospitalization data were gathered by active surveillance, limiting the number of missed hospitalizations. A particular strength of this study was the availability of additional health system data for the subset of participants from Washington County, MD. As such, we were able to test the robustness of our results to using creatinine-based definitions of AKI and time-varying measures of eGFR,

one of the strongest risk factors for AKI. These sensitivity analyses showed the association of higher BMI and elevated WHR with hospitalized AKI to be very robust. The association of BMI and WC with hospitalized AKI was less robust, likely due to the significant correlation between BMI and WC. Limitations of our study included the low rate of hospitalizations for AKI among ARIC participants. BMI and WHR were measured only once at baseline. In addition, only a minority of participants had a WHR below the WHO cut-off which, while potentially limiting our ability to precisely characterize the association between WHR and AKI, may more accurately reflect the U.S. population. As in all observational studies, the relationship between obesity, elevated WHR, and AKI may simply represent confounding, whereby obesity and elevated WHR are present in sicker individuals, who are at higher risk for AKI.

In summary, this study demonstrates an association of elevated BMI and higher WHR with hospitalized AKI independent of baseline kidney function and other known risk factors for AKI. This suggests that in addition to overall adiposity, weight distribution may be important in determining risk of AKI. Strategies to prevent AKI should be considered in individuals with high BMI or high WHR.

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<b>Table 1. Baseline Characteristics by BMI and WHR<sup>1</sup></b>						
<b>Characteristic</b>	<b>BMI</b>		<b>p-value</b>	<b>WHR<sup>2</sup></b>		<b>p-value</b>
	<b>&lt; 30 kg/m<sup>2</sup> (N = 7,193)</b>	<b>≥ 30 kg/m<sup>2</sup> (N = 3,870)</b>		<b>Below cut-off (N = 2,396)</b>	<b>Elevated (N = 8,667)</b>	
Mean age (SD)	63.6 (5.7)	62.8 (5.5)	< 0.001	62.6 (5.7)	63.5 (5.6)	< 0.001
Male (%)	46.2	40.1	< 0.001	55.2	41.0	< 0.001
Black (%)	17.6	30.2	< 0.001	25.2	21.1	< 0.001
Diabetes (%)	11.3	26.8	< 0.001	8.3	19.1	< 0.001
Hypertension (%)	40.9	59.0	< 0.001	36.1	50.3	< 0.001
Coronary heart disease (%)	8.4	8.4	0.9	8.3	8.4	0.8
Mean eGFR in ml/min/1.73 m <sup>2</sup> (SD)	86.1 (15.1)	86.9 (17.1)	0.009	86.9 (15.0)	86.2 (16.0)	0.05
eGFR < 60ml/min/1.73 m <sup>2</sup> (%)	5.6	7.1	0.001	4.5	6.6	< 0.001
No albuminuria (%)	93.0	89.7	< 0.001	94.1	91.2	< 0.001
Moderately increased albuminuria <sup>3</sup> (%)	5.7	8.1		5.0	7.0	
Severely increased albuminuria <sup>4</sup> (%)	1.3	2.2		0.9	1.8	
BMI ≥ 30 kg/m <sup>2</sup>	0	100	N/A	11.0	41.6	< 0.001
<sup>1</sup> BMI and WHR examined independently in 11,063 participants						
<sup>2</sup> Waist-to-hip ratio cut-off for women was 0.85, for men 0.95.						
<sup>3</sup> 30-30 mg of albumin/gram of creatinine.						
<sup>4</sup> > 300 mg of albumin/gram of creatinine.						

<b>Table 2. Cox Proportional Hazard Ratios for Hospitalization for AKI, Overall and by CKD Status</b>				
<b>Group</b>	<b>N</b>	<b>aHR (95% CI); p-value</b>		
		<b>BMI &lt; 30 kg/m<sup>2</sup></b>	<b>BMI ≥ 30 kg/m<sup>2</sup></b>	<b>WHR</b>
Whole cohort	11,063	0.97 (0.94, 1.00); 0.04	1.07 (1.06, 1.09); <0.001	1.03 (1.01, 1.04); <0.001
eGFR < 60ml/min/1.73 m <sup>2</sup> or eGFR ≥ 60ml/min/1.73 m <sup>2</sup> with ACR ≥ 30 mg/g				
No	9,659	0.98 (0.95, 1.02); 0.4	1.08 (1.05, 1.10); <0.001	1.03 (1.01, 1.04); 0.002
Yes	1,404	0.94 (0.90, 0.99); 0.02	1.07 (1.03, 1.10); <0.001	1.02 (1.00, 1.05); 0.05

<b>Table 3. AKI Incidence (95% CI) by BMI and WHR (per 1,000 person years)</b>				
		BMI		
		< 25 kg/m <sup>2</sup>	25-29.9 kg/m <sup>2</sup>	≥ 30kg/m <sup>2</sup>
WHR	Below cut-off	2.9 (2.1, 3.6)	3.0 (2.0, 4.0)	4.2 (2.2, 6.2)
	Elevated	3.6 (2.8, 4.4)	4.2 (3.3, 4.5)	6.3 (5.5, 7.2)
Incidence rates for Caucasian females of mean age of cohort				

<b>Table 4. Cox Proportional Hazard Ratios for Hospitalization for AKI for Sensitivity Analyses</b>				
<b>Group</b>	<b>N</b>	<b>aHR (95% CI); p-value</b>		
		<b>BMI &lt; 30 kg/m<sup>2</sup></b>	<b>BMI ≥ 30 kg/m<sup>2</sup></b>	<b>WHR</b>
Whole cohort	11,063	0.97 (0.94, 1.00); 0.04	1.07 (1.06, 1.09); <0.001	1.03 (1.01, 1.04); <0.001
Addition of hospitalizations as time varying covariate	11,063	0.97 (0.94, 1.00); 0.08	1.07 (1.05, 1.09); <0.001	1.03 (1.01, 1.04); 0.001
Exclusion of AKI occurring during hospitalizations with cardiac procedure	10,978	0.96 (0.93, 0.99); 0.01	1.08 (1.06, 1.10); <0.001	1.03 (1.01, 1.04); <0.001
Identification of AKI using KDIGO creatinine criteria in Washington County participants	2,486	1.00 (0.95, 1.05); 0.9	1.05 (1.02, 1.08); 0.002	1.03 (1.00, 1.06); 0.02
Addition of eGFR as time varying covariate in Washington County participants	2,486	1.00 (0.95, 1.05); 0.9	1.07 (1.04, 1.10); <0.001	1.02 (1.00, 1.05); 0.1

Figure 1. Relationship between BMI and Relative Hazard of Hospitalization with AKI

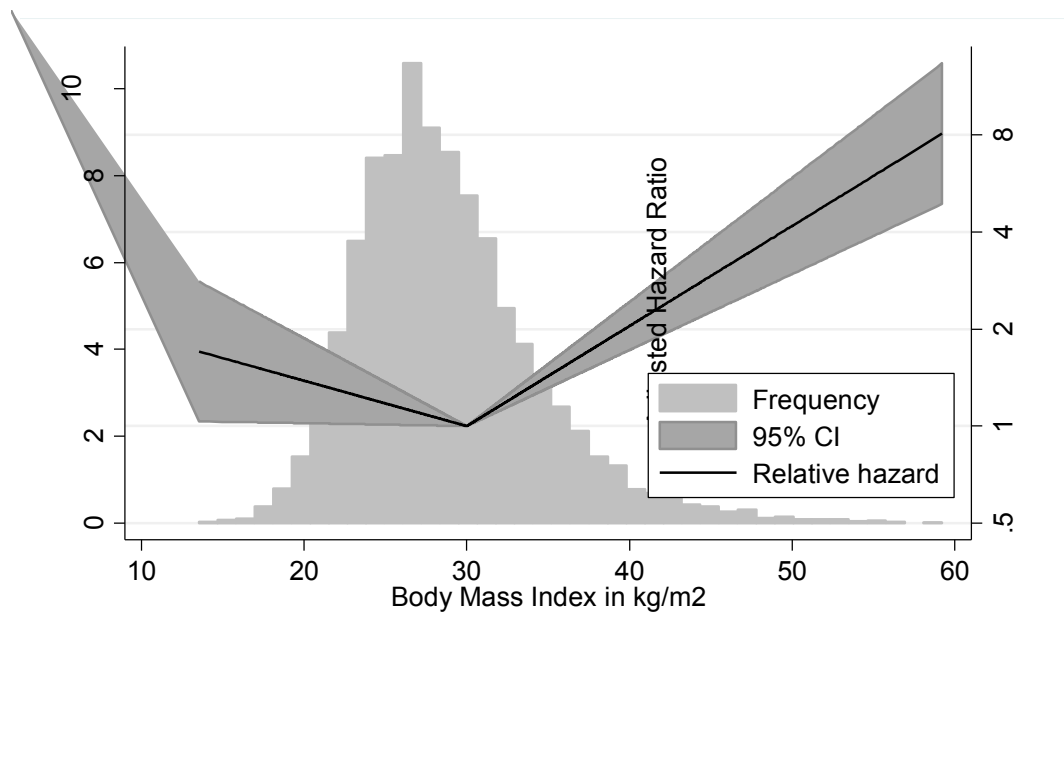
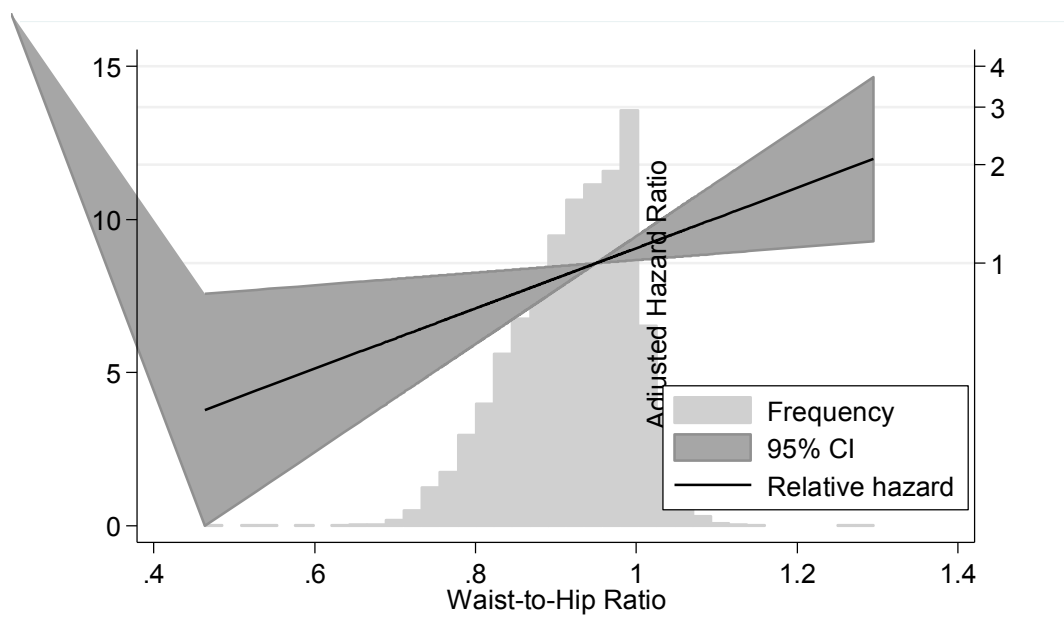


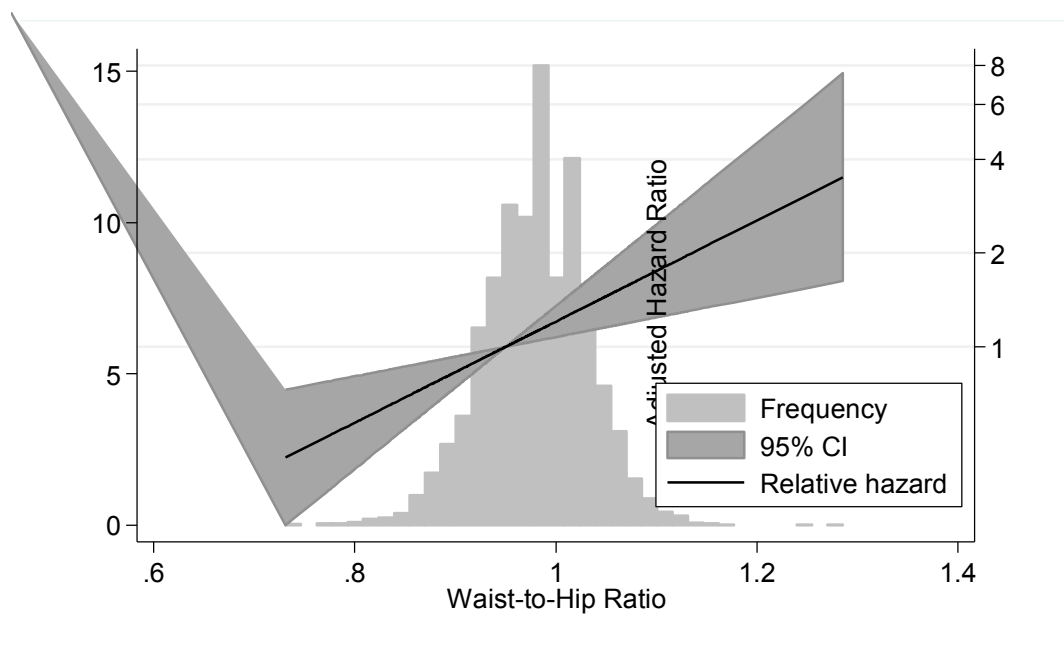


Figure 2. Relationship between WHR and Relative Hazard for Hospitalization with AKI

a. Among Women



b. Among Men



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**MEDICAL TRAINING/EDUCATION**

**JOHNS HOPKINS HOSPITAL**, Baltimore, MD  
**Clinical Fellow**, Division of Nephrology, July 2012 – present

**JOHNS HOPKINS BLOOMBERG SCHOOL OF PUBLIC HEALTH**, Baltimore, MD  
**Master of Health Science** degree candidate in Clinical Epidemiology, expected June 2015  
**Trainee**, T32 Renal Disease Epidemiology Training Grant, July 2013 – June 2015

**JOHNS HOPKINS HOSPITAL**, Baltimore, MD  
**Resident**, Osler Medical Housestaff Training Program, July 2009 – June 2012

**UNIVERSITY OF VIRGINIA SCHOOL OF MEDICINE**, Charlottesville, VA  
**M.D.**, May 2009

- Junior AOA election, 2007
- Merck Manual Award winner (awarded to top 3 students in the first two years), 2007
- Volunteered 100 hours at Recordings for the Blind and Dyslexic (now Learning Ally), 2009

**HARVARD UNIVERSITY**, Cambridge, MA  
**B.A.**, Biology cum laude, 1998

- Harvard College Scholarship, 1994-1998
- Ivy League/Eastern Intercollegiate Swimming League Champion in 50 Yard Freestyle, 1996

**RESEARCH ACTIVITIES**

**WELCH CENTER FOR PREVENTION, EPIDEMIOLOGY, AND CLINICAL RESEARCH, JOHNS HOPKINS UNIVERSITY**, Baltimore, MD  
Risk factors for acute kidney injury, 2013 – present

**JOHNS HOPKINS HOSPITAL**, Baltimore, MD  
**Ad Hoc Peer Reviewer**, 2014 – present

**JOHNS HOPKINS HOSPITAL**, Baltimore, MD  
Recurrence of FSGS after renal transplantation – 2011

**MEMORIAL SLOAN-KETTERING CANCER CENTER**, New York, NY  
**Summer Research Fellow**, Urology, June – August 2006

**PUBLICATIONS**

**Greenberg KI**, McAdams-DeMarco MA, Kottgen A, Appel LJ, Coresh J, Grams ME. “Plasma Urate and Risk of a Hospital Stay with AKI: the Atherosclerosis Risk in Communities Study.” Clin J Am Soc Nephrol. 2015 Feb 25. [Epub ahead of print]

**Greenberg KI**, Perazella MA, Atta MG. “HIV and HCV Medications in End Stage Renal Disease.” *Semin Dial.* 2015 Apr 6. [Epub ahead of print]

### **ORAL PRESENTATIONS**

**Greenberg KI**, Coresh J, Grams ME. “Obesity, weight distribution, and the risk of acute kidney injury in the Atherosclerosis Risk in Communities (ARIC) Study.” Presented at the Mid-Atlantic Nephrology Young Investigator’s Forum in Alexandria, VA, on March 19, 2014.

**Greenberg KI**, Coresh J, Grams ME. “Obesity, weight distribution and the risk of acute kidney injury: the ARIC Study.” Presented at the American Society of Nephrology Annual Meeting on November 15, 2014.

### **EDUCATIONAL ACTIVITIES**

#### **JOHNS HOPKINS HOSPITAL, Baltimore, MD**

**Fellow Member, Division of Nephrology Fellowship Program Review Committee**, 2014

- Assisted Nephrology Fellowship Program Director in reviewing program evaluations by fellows and faculty, and addressing areas needing improvement in the program

#### **JOHNS HOPKINS UNIVERSITY SCHOOL OF MEDICINE, Baltimore, MD**

**Course Faculty**, Genes to Society Renal Course, September 2013 and September 2014

- Led small group discussions and journal club for second year medical students

#### **JOHNS HOPKINS HOSPITAL, Baltimore, MD**

**Fellow Education Coordinator**, Division of Nephrology, 2013 – 2014

- Organized and scheduled semiweekly lectures for fellows throughout the academic year

### **PRIOR WORK EXPERIENCE**

#### **PERLEGEN SCIENCES, INC., McLean, VA**

**Senior Alliance Manager**, private genomics firm, March 2003 – July 2005

- Managed relationships with pharmaceutical partners
- Developed grant applications and contract proposals submitted to NIH and non-profit foundations

#### **BRISTOL-MYERS SQUIBB CO., Lawrenceville, NJ**

**Associate Manager**, Strategic Analysis, Business Development divisions, February 2000 – December 2002

- Assessed market opportunities, monitored key competitors, gathered competitive intelligence, and developed reports and presentations

#### **HEALTH ADVANCES, INC., Wellesley, MA**

**Analyst**, healthcare strategy consulting firm, September 1998 – January 2000

- Worked with pharmaceutical, biotechnology, medical device and diagnostic companies
- Conducted competitive, customer and market analyses; clinician and customer interviews

### **BOARD CERTIFICATION**

Certification in Internal Medicine, American Board of Internal Medicine, October 2012

## **MEMBERSHIPS AND HONORARY/PROFESSIONAL SOCIETIES**

Alpha Omega Alpha

American Medical Association, 2006 – present

American Society of Nephrology, 2010 – present

- Awarded travel support to attend ASN 2011 Annual Meeting
- Awarded travel support to attend 2014 Professional Development Seminar